REMARKS/ARGUMENTS

The Specification has been revised to more expressly recite the subject matter originally presented at the bottom of page 16. The specific sequences that are introduced by the above amendment to the specification were disclosed originally and expressly in their entireties by sequence R_1-X_1-X_2-X_3-X_4-R_2 (I) presented on page 16. To emphasize this disclosure, however, the relevant paragraph on page 16 is now revised to recite each sequence encompassed by sequence R_1-X_1-X_2-X_3-X_4-R_2 (I). No new matter has been introduced, and entry of the amendment to the specification is respectfully requested.

Claims 1, 3, 4, 8, 10, 46, and 47 have been revised to utilize the phrase "consisting of" or "consists of" in place of "comprising" or "comprises" at the start of the claims. Claims 1, 4, 8, and 46 have also been revised to state that the peptides bind $\alpha 3\beta 1$ integrin (with claim 4 having been re-written in independent form), which is supported by the instant application at least on page 11, lines 27-30, and to remove extraneous recitations of "peptide". Claim 1 has also been revised to correct clerical informalities in language. Claim 8 has also been revised to correct typographical oversights and in a manner analogous to claim 1, with subject matter having been moved to new claim 53. New claim 54 is dependent from claim 53 and analogous to claim 9. These revisions are not made in acquiescence of any rejection of record but rather is made to better tailor the claims to currently contemplated clinical embodiments of the invention. Accordingly, the revision is made for reasons related to commercial and business considerations rather than any issue of patentability.

Claims 1, 5 and 8 have also been revised to delete reference to serine at position X_1 and SEQ ID NO:52 based on the telephonic discussions of December 20, 2004 and January 26, 2005 in which Examiner Haddad explained the scope of the search that had been conducted. Claims 1 and 8 have also been revised to more expressly recite certain sequences within the scope as previously presented in the claims. These sequences correspond to certain of the sequences present via the above amendment to page 16 of the specification. Applicants respectfully point out that these changes to claim 1 obviate the need to include any reference to

SEQ ID NOS:12 and 54 in claim 1. As the Examiner is no doubt aware, subject matter corresponding to SEQ ID NO:54 from claim 1 was moved to claim 46 and 47. Similarly, subject matter corresponding to SEQ ID NO:54 in claim 8 is now presented in claims 53 and 54.

Claim 5 has also been revised so as to correspond to revised claim 1.

Claim 46 has been revised to introduce the appropriate Sequence Identifier without altering the scope of the claim.

Claims 2 and 9 have been revised to recite the intended scope wherein the tetrameric sequence is present in the peptides of the claims. The scope of claims 2 and 9 have not been changed because they necessarily had all the limitations of claims 1 and 8, from which claims 2 and 9 depend, respectively. Additionally, the claims have been revised to refer to "up to 12 amino acids in length" based upon the revisions to claims 1 and 8, which are directed to peptides from 5 to 13 amino acids in length. Support is provided in claims 2 and 9 as originally presented.

Claim 7 has been revised to be consistent with revised claim 1.

Claims 11, 12, 15-19, and 31-45 have been canceled as being directed to non-elected inventions. Applicants reserve the right to re-present them in a divisional or other continuing application without prejudice.

Claims 13 and 14 have been revised based upon helpful suggestions from Examiner Haddad on December 20, 2004.

Claims 20, 21, 23-26, and 28-30 remain pending because they are subject to rejoinder as discussed below. Claims 20, 26, 29, and 30 have been revised to be directed to "*in vitro*" methods without any acquiescence to any rejection of record. Instead, the changes are made to better tailor the claims to currently contemplated embodiments of the invention. Accordingly, the revision is made for reasons related to commercial and business considerations rather than any issue of patentability. Claims 22 and 27 have been canceled to correspond to the revisions to claims 20 and 26.

New claims 48-52, all dependent from claim 46, have been introduced. These claims correspond to claims 2, 3, 7, 13, and 14 and reflect claimed subject matter when the

content of claim 46 was previously present in claim 1. Applicants respectfully submit that these new claims require no additional consideration and ask that they be considered and allowed along with claim 46.

New claims 53 and 54 correspond to the subject matter of claims 8 and 9 which were excluded by the revision of claim 8. They are analogous to claims 46 and 47. Applicants respectfully submit that these new claims require no additional consideration and ask that they be considered and allowed along with claims 8 and 9.

No new matter has been introduced, and entry of the amendments is respectfully requested.

Initial Comments

In the interest of clarity in the record, Applicants respectfully and briefly summarize their understanding of the prosecution of the instant application. The Office Action mailed March 24, 2005 has vacated the Action mailed September 24, 2004. Prosecution is proceeding as if Applicants response of August 21, 2004 was the last Applicant communication in the instant application. As such, all Applicants' submissions between August 21, 2004 and March 24, 2005 were not entered. Therefore, Applicants respectfully point out that some of the instant response will repeat positions and arguments previously submitted between August 21, 2004 and March 24, 2005. In some instances, however, reference to a previously submitted response of record will be made to avoid unnecessary duplication of content

Request for Reconsideration of Finality of the Action Mailed March 24, 2005

Applicants have carefully reviewed the Action mailed March 24, 2005 and respectfully point out that contrary to the assertion that "Applicant's amendment necessitated the new ground(s) of rejection", there was at least one new grounds of rejection that was not necessitated by amendment. Accordingly, the "finality" of the Action is premature and should be withdrawn.

As set forth at MPEP 706.07(a), finality in a second or subsequent action occurs "except where the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c)...." Moreover, and as set forth in an "Examiner Note" in MPEP 706.07(a), "a final rejection is improper where there is another new ground of rejection introduced by the examiner which was not necessitated by amendment to the claims."

The Action mailed March 24, 2005 includes a rejection of claims 8 and 9 under 35 U.S.C. § 103(a) as allegedly "unpatentable over Prater et al., Miles et al., WO 92/09628 or USP 6,020,312 in view of USP 5,770,563 (all of record)." Claim 8, however was not amended in Applicants' response of August 21, 2004, and claim 9 was only revised to expressly include an additional recitation of "amino acid" to emphasize the subject matter of the claim.

The previous Office Action, mailed May 21, 2004, only rejected claim 8 based on Prater et al. in view of USP 5,770,563 (see pages 8-9, paragraphs 19-20, of that Action). There were also rejections of claims 8 and 9 under 35 U.S.C. § 102 based on Miles et al. alone, WO 92/09628 alone, and USP 6,020,312 alone. Thus the new rejections of claims 8 and 9, especially in light of the absence of any revision to claim 8, under 35 U.S.C. § 103(a) and on combinations of Miles et al., WO 92/09628 or USP 6,020,312 in view of USP 5,770,563, are all based upon **new grounds** which were not necessitated by amendment. Similarly, the new rejection of claim 9 based upon Prater et al. in view of USP 5,770,563 also relies upon a new ground which was not necessitated by amendment.

In light of the foregoing, Applicants respectfully request reconsideration and withdrawal of the finality of the Action.

Telephonic Interviews of November 17, 2004 and December 20, 2004

Applicants respectfully direct the Examiner's attention to the response filed December 23, 2004 for a summary of the above described interviews.

Telephonic Interview of February 17, 2005

Examiner Haddad explained the status of the instant application and how a new Office Action would issue (with a vacating of the Action mailed September 24, 2004) if Applicants did not direct the claims essentially to the subject matter of claim 4. Applicants declined to so revise the claims and so were told that the previous Action mailed September 24, 2004 was vacated such that no further response was due. Applicants were instructed to await a new Action, which would be made "final" based upon amendments that necessitate new grounds of rejection.

Rejoinder

Claims 20, 21, 23-26, and 28-30 remain directed to methods comprising the use of a peptide according to claim 1 (claims 20, 21, 23-26, and 28-29) or claim 2 (claim 30). As such, they have all the limitations of elected claims 1 and 2 and are subject to rejoinder as set forth at MPEP 821.04. Applicants respectfully ask that claims 20, 21, 23-26, and 28-30 be rejoined and allowed along with claims 1 and 2.

Claim Objections

Claim 46 was objected to under 37 CFR 1.821(d) because it lacks a sequence identifier. Applicants respectfully request withdrawal of this objection in light of the amendment to claim 46.

Claim Rejection under 35 U.S.C. § 112, second paragraph

Claims 2, 5 and 9 were rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite.

Claims 2 and 9 were rejected for reciting "from about 4 to about 12 amino acids" because "[i]t is unclear how many amino acids constitute 'about'".

Applicants respectfully, but strongly, traverse the instant rejection as failing to present a *prima facie* case of indefiniteness for the reasons provided in the last response.

Specifically, it is well settled law that the term "about" is not indefinite *per se*. This standard was not applied in the instant situation, which is appears to be based upon the view that "about 12" is indefinite in the absence of a definition (and thus *per se* indefinite).

However, and in light of the revisions to claims 1 and 8 to use "consisting of" as the transitional phrase, "about 12" is delimited by the maximum length of 13 as provided for by the literal scope of the claims. Accordingly, the claims have been revised to recite "up to 12 amino acids" in the interest of advancing prosecution of the instant application. Applicants thus respectfully submit that the instant rejection has been obviated and so withdrawal is requested.

Claim 5 was rejected as allegedly indefinite for lack of antecedent basis for "X_1-X_2-X_3-X_4". The claim as been revised to correspond to revised claim 1 as presented above. Applicants respectfully submit that this rejection has been obviated and so may be withdrawn.

Claim Rejections under 35 U.S.C. § 112, first paragraph

Claims 1-5, 7-10, 13, 14, 46, and 47 were rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to "reasonably provide enablement for any peptide 'comprising'" the sequences recited in claims 1, 8 and 46.

As an initial matter, Applicants respectfully submit that no issue of non-enablement exists in light of the claim revisions provided above, which exclude the use of "comprising" and include the statement that the peptides bind $\alpha 3\beta 1$ integrin. Accordingly, Applicants believe that no *prima facie* case of undue experimentation exists, especially in light of the standard set out in part at MPEP 2164.04, including *In re Marzocchi*[1] and the other cases cited therein.

Once again, Applicants point out that no objective reason has been provided to question that undue experimentation is needed to make and use the claimed peptides, which are now of defined lengths, as encompassed by the revised claims.

[1] 439 F.2d 220, 169 USPQ 367 (CCPA 1971).

To the contrary, the instant invention is similar to the situation seen with a common integrin binding motif, Arg-Gly-Asp (RGD) as discovered via fibronectin. In the case of the RGD sequence, there is no reason to doubt that it is possible to make and use a variety of peptides containing the sequence, which retain the ability to bind integrin, without undue experimentation. This follows because while there may be some unpredictability as to whether some peptides having the RGD sequence will misfold as to present a structure that will not bind integrin, the amount of experimentation necessary to address this unpredictability is not undue.

The instant invention is directed to an analogous situation because no objective reasons have been provided as to why the instant tetrameric sequence, as recited in claims 1, 8, and 46, cannot be treated in the same manner as the RGD sequence known in the art. Both sequences are in the same, and more specific, field of integrin binding peptides. Accordingly, the reliance upon the articles by Kuntz et al. and Miller et al. (in the previous Office Action mailed May 21, 2004) is misplaced because the content of both fail to take either the RGD sequence or the instant tetrameric sequence into consideration. Instead, the content of both paint a picture of the situations with other proteins and polypeptides that are unrelated to the peptides of the invention. Accordingly, Applicants respectfully submit that the contents of those references are not dispositive relative to the instant application.

A much more relevant comparison to the instant application is present in *In re Wands*[2] (copy attached), where no undue experimentation was present to support an assertion of a lack of enablement. The facts of *Wands* involve claims directed to immunoassays to detect hepatitis B surface antigen (HBsAg) by use of monoclonal antibodies (MAb)which bind the antigen, wherein the MAb have a high affinity of at least 10^{-9} M for the antigen. The claims were solely rejected as requiring undue experimentation to make the MAb needed to practice the invention. The Patent and Trademark Office (PTO) took the position that "data presented by Wands show that the production of high affinity IgM anti-HBsAg antibodies is unpredictable and unreliable."[3] There was no issue of "how to use" the *Wands* invention because, like in the

[2] 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

instant application where one skilled in the art would know how to use the peptides to bind α3β1 integrin as disclosed, one skilled in the art would know how to use the high affinity MAb in the claimed immunoassays.

The Federal Circuit accepted the Wands argument that "methods to make high-affinity IgM anti-HBsAg antibodies requires only routine screening, and that does not amount to undue experimentation."[4] More specifically, the Federal Circuit stated clearly that "[e]nablement is not precluded by the necessity for some experimentation such as routine screening."[5] The court then continued by reviewing the process for producing monoclonal antibodies by use of hybridoma cells followed by the following:

> The nature of monoclonal antibody technology is that it involves screening hybridomas to determine which one secrete antibodies with desired characteristics. Practitioners of this art are prepared to screen negative hybridomas in order to find one that makes the desired antibody.... Furthermore, in the monoclonal antibody art it appears that an 'experiment' is not simply the screening of a single hybridoma but is rather the entire attempt to make a monoclonal antibody against a particular antigen.... Wands carried out this entire procedure [to make a monoclonal antibody] three times, and was successful each time in making at least one antibody that satisfied all of the claim limitations.[6]

The Federal Circuit then proceeded to conclude that no undue experimentation was needed to obtain antibodies to practice the claimed invention.

The facts and law in *Wands* are directly applicable to the instant invention because like MAb, the claimed peptides are polypeptides that bind a target molecule (HBsAg in *Wands* and α3β1 integrin in the instant invention). The situations are also similar in the sense

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[3] *Id.* at 1402.

[4] *Id.* at 1404.

[5] *Id.*

[6] *Id.* at 1406-7.

that like the MAb situation, the claimed peptides are not prepared by an "experiment" that is simply the screening of a single peptide. To the contrary, the instant peptides can be prepared in combinations such that multiple peptides are prepared and screened simultaneously where the skilled artisan is prepared to screen "negative" peptides that do not have $\alpha 3\beta 1$ integrin binding activity.

This latter parallel between *Wands* and the instant application is demonstrated not only by the peptides shown on page 34, Table 2, of the application, but also by the results of alanine scanning across the binding sequence as shown on page 36, Table 3. Table 3 shows that substitution of an alanine (alanine scanning mutagenesis) for 9 of 12 positions[7] in a dodecameric peptide containing the NVRF tetrameric sequence, the binding affinity is unchanged for positions outside the tetrameric NVFR core motif. Accordingly, one skilled in the art presented with these results would expect that the majority, if not all, of positions outside the tetrameric core motif may be substituted with other amino acid residues without deleterious effects on binding to $\alpha 3\beta 1$ integrin. *The instant statement of the rejection provides no objective reason to counter this view.* Moreover, and because the facts of *Wands* are so much more applicable to the instant application, no reliance on *In re Fisher* is acceptable where it is differs from the situation in Wands and the instant invention.

Therefore, and to the extent that any residual concern may be present with respect to enablement for the revised claims based upon a possible need for screening assays or the definitions of the R_1 and R_2 groups in the claims, Applicants respectfully submit that as previously explained, no more than routine and repetitive experimentation, like that in *Wands*, is needed to make and use the instantly claimed invention.

This position is also applicable to claims 13 and 14 (as well as new claims 51-52) because contrary to the statement of the rejection, the instant application describes the use of peptides to inhibit vascularization in a chick chorioallantoic membrane, or CAM, (see pages 47-48, Table 5) as well as modulate endothelial cell and SCLC proliferation and other behavior (see

[7] The three unsubstituted positions are those occupied by Gly (third residue), Val (fourth residue), and Val (eleventh residue), which are already small side chain residues like alanine.

pages 40-46). The correlation between a CAM assay and angiogenesis is well known such that the former is used as a screen to increase the expectation of successfully using a molecule to inhibit the latter. The ability to inhibit cell activities *in vitro* provides a reasonable basis to support the claims as filed.

Given the guidance provided by the instant application and the absence of objective reasons to doubt the presence of an enabling disclosure given the disclosure as provided, the claimed invention must be **presumed enabled**. Accordingly, Applicants respectfully request withdrawal of the instant rejection.

Claims 1-5, 7-10, 13, 14, 46 and 47 were rejected under 35 U.S.C. § 112, first paragraph as allegedly "failing to comply with the written description requirement." Applicants have carefully reviewed the statement of the instant rejection and respectfully traverse because no *prima facie* case of an inadequate written description has been presented.

As an initial matter, Applicants point out that the statement of the rejection asserts that

> there is no described or art-recognized correlation or relationship between the structure of the invention, the generic formulae and it's anti-angiogenic, anti-proliferation function (i.e., inhibition of a $\alpha 3\beta 1$/TSP interaction), the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed genus of variants which retain the features essential to the instant rejection. (see page 6 of the previous Office Action)

Applicants respectfully submit that contrary to the position reflected by the above quote, the instant application clearly asserts that the disclosed tetrameric core motif is responsible for (or correlated with) the activities of the invention as disclosed. Moreover, Applicants strongly disagree with the apparent assertion that the correlation needs to be "art-recognized". How can this be the standard? Is it not possible for an application, like the instant one, to disclose a correlation between structure and function for the first time? Applicants

respectfully submit that this possibility must be available and so the view taken in the instant rejection cannot stand.

Additionally, the above quote seems to admit that the instant application discloses at least anti-angiogenic and anti-proliferative uses of the claimed invention in relationship to $\alpha 3\beta 1$ integrin binding. This is at odds with the rejection addressed above, which asserted that no such properties were available for the use of the compositions of claims 13 and 14 (as well as claims 51 and 52).

To the extent that this rejection is based upon the view that amino acid residues in the R_1 and R_2 groups must be defined to provide a written description, Applicants strongly disagree because the invention is based upon the tetrameric core motif as claimed. This is supported by the data on page 36, Table 3. Applicants believe that it is improper for the Office to redefine the invention to be something other than that which Applicants claim.

In light of the above, as well as the **strong presumption** of an adequate written description as discussed in the previous response, Applicants simply do not believe that any issue of an inadequate written description is present. Accordingly, withdrawal of this rejection is respectfully requested.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 8 and 9 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Prater et al., Miles et al., WO 92/09628 or USP 6,020,312 in view of USP 5,770,563 (all of record)." Applicants have carefully reviewed the statement of the instant rejection and point out that as explained above, this rejection is based in part on new grounds not necessitated by amendment.

Claim 8 has been revised in a manner analogous to claim 1. Accordingly, the limitations of claim 8 are not taught, suggested, or otherwise indicated by any of Prater et al., Miles et al., WO 92/09628 or USP 6,020,312, or any combination of these four primary references. Moreover, USP 5,770,563 fails to remedy this deficiency of the four primary

references. Applicants respectfully submit that this rejection has been obviated and so may be withdrawn.

"New Matter" Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-3, 5, 7, 13, 14, and 46 were rejected under 35 U.S.C. § 112, first paragraph as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection."

Applicants have carefully reviewed the statement of the instant rejection and respectfully submit that no *prima facie* case of an inadequate written description due to "new matter" has been presented.

The instant rejection asserts that claims 1 and 46 create "a new subgenus of peptides" that are not adequately disclosed by the description of a genus of peptides by sequence R_1-X_1-X_2-X_3-X_4-R_2 (I) on page 16 of the instant application and as originally recited in claim 1. Relying upon *In re Smith*,[8] the rejection asserts that a "subgenus is not necessarily implicitly described by a genus encompassing it and a species upon which it reads." A review of *Smith* shows that the holding was made in rejection of an appellant argument that "disclosure of a genus and a species of a subgenus is a sufficient description of the subgenus".[9] But the instant application does not rely upon the rejected appellant argument. To the contrary, the instant application and claims differ significantly from *Smith*.

Specifically, and contrary to the statement of the rejection, the instantly revised claims are directed to specific sequences that are each disclosed in the instant application. Thus

[8] 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972), which also states that "[p]recisely how close the description must come to comply with § 112 must be left to case-by-case development." This indicates that *Smith* can only be applied narrowly based on its precise facts and arguments.

[9] *Id.*

the claims may be viewed as directed to individual species, each of which are disclosed. To the extent that a "subgenus" may be present in the claims, such a "subgenus" is simply the inclusion of more than one disclosed species in a single claim. Therefore, and very different from *Smith*, the instant application is not one where claims are re-directed to a subgenus based on disclosure of only a genus and one species of the subgenus. To the contrary, the instant application provides a disclosure of a genus (defined by sequence R_1-X_1-X_2-X_3-X_4-R_2 (I) on page 16 and original claim 1 of the instant application) made up of specific species, each of which are disclosed. The claims are now being directed to particular species as disclosed (and as within the scope of the disclosed genus).

To emphasize the distinction between the facts of the instant application and the position of in the instant rejection, sequence R_1-X_1-X_2-X_3-X_4-R_2 (I) on page 16 of the application has been revised to expressly list all the species encompassed thereby. Claims 1 and 8 are now directed to five of those species (N-V-R-L, SEQ ID NO:57; N-V-R-F, SEQ ID NO: 51; Q-V-R-L, SEQ ID NO: 80; Q-V-R-F, SEQ ID NO:53; and D-V-R-L, SEQ ID NO:102) while claim 46 and 53 are directed to only one of those species (DVRF, SEQ ID NO:54).

The revised claims are in sharp contrast to the instant rejection's assertion that they "recite[] a limitation which was not clearly disclosed in the specification and recited in the claims as originally filed". This follows because the claims are directed to species that were within the scope of the claims as originally presented and within the disclosure of the instant application as originally filed. The species now claimed are also supported by specific working examples of peptide species in Tables 2, 3, and 5 of the instant application.

Applicants also wish to point out that the instant application is more appropriately viewed as one where the specification discloses a genus composed of a plurality of specific, and disclosed, species. Given this, Applicants may properly amend claims directed to the genus by subtracting member species of the genus. See *In re Johnson*.[10] In *Johnson*, the court made clear that, "[i]t is for the inventor to decide what bounds of protection he will seek," and that

[10] 194 USPQ 187 (CCPA 1977).

"substantially eliminating the right of an applicant to retreat to an otherwise patentable species " would essentially "let form to triumph over substance."[11] The revisions to claims 1 and 8, as well as the presentation of new claims 46 and 53, are merely decisions by Applicants to focus the bounds of protection on particular species rather than the original genus.

Accordingly, Applicants respectfully submit that no *prima facie* case has been presented and this rejection may be properly withdrawn.

Claim Rejections under 35 U.S.C. § 102

Claims 1-2, 5, and 13-14 were rejected under 35 U.S.C. § 102(a) as allegedly anticipated by JP10-25896 (9/1998). This rejection was discussed during a previous telephonic interview because the actual teachings of the cited reference were unclear in the absence of a translation of the relative portions of the document. For example, it is unclear whether the sequence in the reference as relied upon is merely a portion of a larger sequence.

While Examiner Haddad will endeavor to obtain a translation of the cited reference, Applicants point out that this rejection is not applicable to the revised claims, which no longer recite "comprising". Accordingly, this rejection may be properly withdrawn.

Claims 1-2 and 5 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Fowlkes et al. (USP 5,789,184).

Applicants have carefully reviewed the statement of the instant rejection and respectfully point out that the reference fails to actual disclose a peptide. Fowlkes et al. only describe the isolation of plasmids containing particular sequences that are manually interpreted as encoding the sequence of SEQ ID NO:55 in the reference (see column 61, lines 40-59). This is not a disclosure of an actual peptide having that sequence because no such peptide is taught to exist. Applicants respectfully submit that it is entirely possible that the peptide is not expressed or is expressed as a larger or truncated version. Simply put, it is not clear whether a peptide

[11] See *id.* at 196.

having only SEQ ID NO:55 is actually in existence based on the cited reference. Accordingly, no *prima facie* case of anticipation has been presented.

Moreover, Applicants point out that this rejection is not applicable to the revised claims, which no longer recite "comprising". This presents a second reason why no *prima facie* case is present. Accordingly, this rejection may be properly withdrawn for both of these reasons.

Claim Rejections under 35 U.S.C. § 103(a)

Claims 7-9 and 13-14 were rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over either of JP10-25896 or Fowlkes et al. in view of USP 5,770,563 (Roberts et al.).

Applicants have carefully reviewed the statement of the instant rejection and respectfully submit that no *prima facie* case of obviousness has been presented. As noted above, neither of JP10-25896 and Fowlkes et al. is properly applicable to the claims from which claims 7-9 and 13-14 depend. Accordingly, this rejection may be withdrawn for this reason.

Additionally, Applicants respectfully point out that no adequate reason or motivation has been provided for why an ordinary artisan would combine the references as alleged. The teachings of JP10-25896 are unclear for the reasons provided above. Given no knowledge as to that disclosure, why would one of ordinary skill combine it with the thrombospondin peptides of Roberts et al.? The simple answer is that they would not in the absence of impermissible hindsight reconstruction.

Similarly, why would the ordinary artisan combine the teachings of Fowlkes et al., which relate to yeast pheromone technology, combine them with the thrombospondin peptides of Roberts et al.? Again, there would be no suggestion or motivation without use of impermissible hindsight based on the instant application.

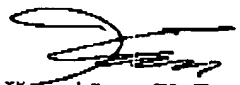
In addition to these reasons, Applicants point out that this rejection is not applicable to the revised claims, which no longer recite "comprising". Accordingly, this rejection may be properly withdrawn for all of these reasons.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 858-350-6151.

Respectfully submitted,



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